

### REMARKS

Reconsideration of the instant application in view of the present amendments and the following remarks is respectfully requested. As of the mailing date of the Final Office Action dated March 20, 2008, claims 5-16 were pending and under examination. By the present amendment, claims 5-16 are canceled without acquiescence to any rejection. New claims 27-37 are added to recite specific embodiments of the present invention. Support for these amendments may be found throughout the specification and claims as originally filed. Support for independent claim 27 is provided, for example, in paragraphs 0126-0136 and Table 3 of the published application (Publication No. 20070042368). Claims 7-16 have been canceled and rewritten as new claims 28-37 in order to avoid dependence from a later claim. As such, support for these claims is found, for example, in the claims as filed. Therefore, the present amendments do not constitute new matter. The present amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Claims 27-37 are now pending and under consideration.

Applicants wish to thank the Examiner and her supervisor for the productive interview conducted via telephone on June 16, 2008, during which the outstanding rejection under 35 U.S.C. § 103 was discussed.

### ***Claim Rejections – 35 U.S.C. § 103***

Claims 5-16 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Henderson *et al.* (20020172952) in view of Wang *et al.* (20020052329; Wang '329) and Wang *et al.* (20020099012; Wang '012) and further in view of Edwards and Gibbs (PCR Methods and Applications, vol. 3, pages S65-S75, 1994). Specifically, the Office asserts that the Henderson *et al.* reference and the two Wang *et al.* references disclose methods for detecting the presence of lung cancer cells and further disclose the individual cancer-associated markers as recited in the present claims. The Office concedes that these references do not teach detecting these markers in a multiplex format. However, the Office asserts that methods for detecting multiple targets in a biological sample were well known in the prior art, as evidenced by

Edwards and Gibbs. As such, the Office asserts that the skilled artisan at the time of the claimed invention, would have been motivated to modify the methods taught in the Henderson *et al.* and the two Wang *et al.* references to encompass the multiplex PCR as taught by Edwards and Gibbs. In response to Applicants' previous arguments, the Office notes that the claims do not require that a combination of specific markers be detected in order to advantageously detect lung cancer.

Applicants respectfully traverse this ground for rejection and submit that the presently claimed methods are not obvious in view of the cited art. Applicants note that claims 5-16 have been canceled and address the present rejection as it may relate to new claims 27-37. The new claims are consistent with the discussions held during the telephone interview of June 16, 2008. In particular, as discussed during the interview, Applicants submit that the cited prior art does not teach or even suggest that the specific combinations of lung tumor markers as presently recited could be used in a method for detecting lung cancer with the advantage of achieving a high specificity of at least 86%. Additionally, contrary to the Office's assertion, nothing in the prior art would have permitted the person having ordinary skill to reasonably predict that the combination of the individual recited cancer-associated markers would provide the advantages of the presently claimed method.

The Supreme Court's decision in *KSR* did not change the obviousness analysis with regard to finding a reasonable expectation of success in the cited art instead of in the Applicant's disclosure. It is respectfully submitted that the subject matter of the instant claims simply could not have been predicted by the prior art, where neither Henderson *et al.*, Wang *et al.* ('329) or Wang *et al.* ('012), each alone or in combination with any other knowledge in the prior art including Edwards and Gibbs, provide the requisite reasonable expectation of success to the person of ordinary skill. On this point, prior to the instant application, it could not be predicted, *e.g.*, whether the detection of the recited cancer-associated markers combined would provide detection of lung cancer with a specificity of 86% or greater. As articulated by the Supreme Court, the presently recited combination thus does "more than yield a predictable result", and is therefore nonobvious.

Accordingly and in view of the foregoing, Applicants submit that the instant claim satisfies the requirements of 35 U.S.C. § 103. Reconsideration and withdrawal of the rejection are respectfully requested.

Applicants respectfully submit that all of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,  
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